General

Guideline Title

Topotecan, pegylated liposomal doxorubicin hydrochloride, paclitaxel, trabectedin and gemcitabine for treating recurrent ovarian cancer.

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Topotecan, pegylated liposomal doxorubicin hydrochloride, paclitaxel, trabectedin and gemcitabine for treating recurrent ovarian cancer. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Apr 27. 61 p. (Technology appraisal guidance; no. 389).

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: National Institute for Health and Clinical Excellence (NICE). Paclitaxel, pegylated liposomal doxorubicin hydrochloride and topotecan for second-line or subsequent treatment of advanced ovarian cancer. London (UK): National Institute for Health and Clinical Excellence (NICE); 2005 May. 46 p. (Technology appraisal; no. 91).

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Paclitaxel in combination with platinum or as monotherapy is recommended within its marketing authorisation as an option for treating recurrent ovarian cancer.

Pegylated liposomal doxorubicin hydrochloride (PLDH) as monotherapy is recommended within its marketing authorisation as an option for treating recurrent ovarian cancer.

PLDH in combination with platinum is recommended as an option for treating recurrent ovarian cancer.[1,2]

The following are not recommended within their marketing authorisations for treating the first recurrence of platinum-sensitive ovarian cancer:

- Gemcitabine in combination with carboplatin
- Trabectedin in combination with PLDH
- Topotecan

The appraisal committee was unable to make recommendations on the use of these technologies for treating platinum-sensitive ovarian cancer beyond the first recurrence.

Topotecan is not recommended within its marketing authorisation for treating recurrent platinum-resistant or platinum-refractory ovarian cancer.

People whose treatment with gemcitabine in combination with carboplatin, trabectedin in combination with PLDH, or topotecan is not recommended in this National Institute for Health and Care Excellence (NICE) guidance, but was started within the National Health Service (NHS) before this guidance was published, should be able to continue treatment until they and their NHS clinician consider it appropriate to stop.

Footnotes

[1]At the time of publication (April 2016), PLDH (Caelyx) in combination with platinum did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing medicines – guidance for doctors for further information.

[2]The use of PLDH (Caelyx) in combination with platinum is outside the terms of the marketing authorisation for Caelyx. Consequently the statutory funding requirement does not apply to this recommendation. NICE received a remit to appraise this combination under Regulation 5 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 .

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Recurrent ovarian cancer

Guideline Category

Assessment of Therapeutic Effectiveness

Treatment

Clinical Specialty

Obstetrics and Gynecology

Oncology

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To assess the clinical effectiveness and cost-effectiveness of topotecan, pegylated liposomal doxorubicin hydrochloride (PLDH), paclitaxel, trabectedin and gemcitabine for the treatment of advanced, recurrent ovarian cancer

Target Population

Women with ovarian cancer that has recurred after first-line (or subsequent) platinum-based chemotherapy or that is refractory to platinum-based chemotherapy

Interventions and Practices Considered

1. Paclitaxel alone or in combination with platinum chemotherapy
2. Pegylated liposomal doxorubicin hydrochloride (PLDH) alone or in combination with platinum chemotherapy

Note: The following were considered but not recommended: gemcitabine, trabectedin in combination with PLDH, topotecan.

Major Outcomes Considered

- Clinical effectiveness
  - Overall survival (OS)
  - Progression-free survival (PFS)
  - Overall response rate (ORR)
  - Adverse effects of treatment
  - Health-related quality of life (HRQoL)
  - Time to progression (TTP)
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The Assessment Report for this technology appraisal was prepared by BMJ-Technology Assessment Group (BMJ TAG) (see the "Availability of Companion Documents" field).

Assessment of Clinical Effectiveness

Methods for Reviewing Effectiveness

Identification of Studies

The literature search for this review was designed to update and expand the systematic search carried out in Technology Appraisal 91 (TA91), which evaluated the clinical and cost-effectiveness of topotecan, pegylated liposomal doxorubicin hydrochloride (PLDH), and paclitaxel. Medical Subject Headings (MeSH) and text terms for ovarian cancer, topotecan, PLDH, and paclitaxel were taken from the search strategy presented in TA91, and text terms added for the interventions trabectedin and gemcitabine. To ensure capture of all potentially relevant studies to inform a network meta-analysis (NMA), the decision was taken not to restrict the start date of the update search to the end date of the search (2004) reported in TA91.

As a result of the large number of studies retrieved from the scoping search, the decision was taken to implement search filters for randomised controlled trials (RCTs). Filters developed and validated by Scottish Intercollegiate Guidelines Network were used. The identified RCTs facilitated construction of three distinct networks for the outcomes of overall survival (OS) and progression-free survival (PFS) for both the platinum-sensitive (two networks) and platinum-resistant/refractory (1 network) subgroups. In an attempt to identify a study to link the discrete networks for the platinum-sensitive subgroup, the retrieved abstracts were re-examined to consider interventions outside the scope of this review. Due to time constraints, the decision was taken not to search for non-randomised trials. Bibliographies of previous reviews and retrieved articles were searched for additional studies. Clinical trial registries were also searched to identify planned, ongoing and finalised clinical trials of interest. In addition, clinical experts were contacted with a request for information on any additional studies of which they had knowledge. The manufacturers' submissions (MSs) were assessed for unpublished data. Although the protocol stipulates that the Index to Scientific and Technical Proceedings would be searched to identify relevant conference proceedings, due to time constraints this was not undertaken. However, based on the conference abstracts retrieved from the search of the pre-specified electronic databases, the Technology Assessment Group (TAG) considers it likely that the key conference abstracts have been identified. Conference abstracts that were reviewed and found not to report additional results to those presented in the relevant full publication were excluded.

Electronic databases were initially searched on 18 January 2013 and results uploaded into Reference Manager Version 11.0 and deduplicated. An update search was carried out on 23 May 2013. No papers or abstracts published after this date were included in the review. Full details of the strategies are presented in Appendix 1 of the Assessment Report.

Titles and abstracts returned by the search strategy were examined independently by two researchers and screened for possible inclusion. Disagreements were resolved by discussion, or involvement of a third reviewer in cases where consensus could not be achieved. Full texts of potentially relevant studies were ordered. Full publications were assessed independently by two reviewers for inclusion or exclusion against prespecified criteria, with disagreements resolved by discussion or input from a third reviewer when consensus could not be achieved.

Inclusion and Exclusion Criteria

For the review of clinical effectiveness, only RCTs were considered for inclusion in the review. Systematic reviews and non-randomised studies were excluded, as were studies that considered drugs administered as "maintenance therapy" following directly on from first-line therapy without evidence of disease progression. Inclusion criteria were based on the decision problem outlined in Section 3.1 of the Assessment Review (presented as a whole in the table below). No restrictions were imposed on language or date of publication. Reference lists of identified systematic reviews were used as a source of potential additional RCTs, as well as a resource to compare studies retrieved from the systematic literature search.

Table: Inclusion Criteria (Based on the Decision Problem) for Studies Evaluating Clinical Effectiveness

	Inclusion Criteria
Study Design	Randomised controlled trials (RCTs)
Population	People with ovarian cancer that has recurred after first-line (or subsequent) platinum-based chemotherapy or is refractory to platinum-based chemotherapy
Interventions	For people with platinum-sensitive ovarian cancer: • Paclitaxel as monotherapy or in combination with platinum-based chemotherapy • Pegylated liposomal doxorubicin hydrochloride (PLDH) as monotherapy or in combination with platinum-based chemotherapy • Gemcitabine in combination with carboplatin • Trabectedin in combination with PLDH • Topotecan monotherapy For people with platinum-resistant or platinum-refractory ovarian cancer: • Paclitaxel as monotherapy or in combination with platinum-based chemotherapy • PLDH monotherapy • Topotecan monotherapy For people with ovarian cancer who are allergic to platinum-based chemotherapy: • Paclitaxel monotherapy • PLDH monotherapy • Trabectedin in combination with PLDH • Topotecan monotherapy

Comparators	**Inclusion Criteria** For people with platinum-sensitive ovarian cancer: • The interventions listed above in comparison with each other • Bevacizumab in combination with platinum-containing chemotherapy (subject to National Institute for Health and Care Excellence [NICE] appraisal) • Single-agent platinum chemotherapy For people with platinum-resistant or platinum-refractory ovarian cancer: • The interventions listed above in comparison with each other • Etoposide as monotherapy or in combination with platinum-based chemotherapy • Best supportive care For people with ovarian cancer who are allergic to platinum-based chemotherapy: • The interventions listed above in comparison with each other • Etoposide monotherapy • Best supportive care

Quantity and Quality of Research Available

The searches retrieved a total of 5,993 records (post deduplication) that were of possible relevance to the review (see Figure 3 in the Assessment Report). These were screened and 104 full references were ordered. Of these 5 had to be cancelled because they were unobtainable. Of the full references evaluated, 28 papers describing 16 studies were included in the review.

The full list of studies included in the review is given in Table 18 of the Assessment Report, while a list of the papers screened but subsequently excluded (with reasons for exclusion) from the review is presented in Appendix 3 of the Assessment Report.

Assessment of Cost-effectiveness

Technology Assessment Group Systematic Review of Existing Cost-effectiveness Evidence

A systematic review was carried out in December 2012 to identify relevant published economic evaluations to support the development of this multiple technology appraisal (MTA). The following databases were searched:

- MEDLINE (Ovid)
- EMBASE (Ovid)
- Health Technology Assessment database (HTA)
- NHS Economic Evaluations Database (NHS EED)

The search strategy for MEDLINE and EMBASE combined terms capturing the interventions and comparators of interest (topotecan, PLDH, paclitaxel, trabectedin, gemcitabine, best supportive care, bevacizumab, carboplatin, cisplatin, and etoposide); the target condition (ovarian cancer); and terms to capture economic evaluations. As this MTA is in part an update of TA91, in which a systematic review was carried out (search date of April 2004) to evaluate the cost-effectiveness of topotecan, PLDH, and paclitaxel, searches for these interventions were carried out with a date limit of 2004. Databases were searched from inception for gemcitabine and trabectedin. The search strategy for HTA and NHS EED combined terms for the target condition (ovarian cancer) with no further limits. Full details of the search terms are presented in Appendix 5 of the Assessment Report.

In addition to searches of the above databases the following sources of potentially relevant publications were explored:

- Experts in the field were contacted with a request for details of relevant published and unpublished studies of which they may have knowledge.
- The NICE Web site was searched for any recently published Technology Appraisals in ovarian cancer that had not already been identified via the database searches.
- Reference lists of key identified studies were reviewed for any potentially relevant studies.

No restrictions on language or setting were applied to any of the searches. The titles and abstracts of papers identified through the searches were independently assessed for inclusion by two health economists using the criteria outlined in the table below.

Table: Inclusion and Exclusion Criteria for the Economic Evaluation Systematic Review

Inclusion Criteria	Exclusion Criteria
• All full economic evaluations (cost-effectiveness, cost-benefit, cost-consequence or cost minimisation) • Any setting (to be as inclusive as possible) • At least one of the interventions or comparators as per the final scope	• Abstracts with insufficient methodological details • Systematic reviews

The systematic review was updated in May 2013 whilst the report was under peer review. The search strategy remained the same as outlined above; however, results were limited from December 4th 2012 to May 21st 2013 in order to identify only additional relevant studies.

A total of 842 papers were identified from the December 2012 search (see Figure 14 in the Assessment Report). Of these papers, 740 were excluded on the basis of title and abstract. A total of 102 papers were therefore identified as potentially relevant and were ordered for full review. Of the 102 ordered papers, 59 were excluded following review of the full paper. For a description of the reason for exclusion of the ordered papers, see Appendix 6 of the Assessment Report. A total of 43 papers were identified as economic evaluations from the December 2012 search.

A further 91 papers were identified from the updated search in May 2013. Of these, 90 were excluded on the basis of title and abstract, with one paper identified as potentially relevant and ordered for full review. Additionally, two relevant NICE TAs were identified from the NICE Web site and were reviewed in full: TA284 and TA285.

Number of Source Documents

Clinical Effectiveness

Of the full references evaluated, 28 papers describing 16 studies were included in the review.

Cost-effectiveness

- Of the 46 economic evaluation studies identified from the December 2012 (43 papers) and May 2013 (three papers) searches, 21 related specifically to recurrent ovarian cancer (see Table 89 of the Assessment Report). These 21 studies were considered by the TAG to be the most relevant to this MTA, and were extracted in full; the remaining included papers are presented as short summaries (see Appendix 7 of the Assessment Report).
- The Assessment Group and one of the manufacturers submitted economic models.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The Assessment Report for this technology appraisal was prepared by BMJ-Technology Assessment Group (BMJ TAG) (see the

"Availability of Companion Documents" field).

Assessment of Clinical Effectiveness

Methods for Reviewing Effectiveness

Data Abstraction Strategy

Data pertaining to study design, methodology, baseline characteristics, and clinical outcomes efficacy were extracted by two reviewers into a standardised data extraction form and validated by a second. Discrepancies were resolved by discussion when necessary. Authors of reports published as meeting abstracts only, where insufficient methodological details were reported to allow critical appraisal of study quality were contacted with a request for additional information. If no additional information was obtained, the studies were excluded. Data extraction forms for the included studies are provided in Appendix 2 of the Assessment Report.

Critical Appraisal Strategy

The quality of the clinical effectiveness data was assessed by two independent reviewers and checked for agreement. The study quality was assessed according to recommendations by the National Health Service (NHS) Centre for Reviews and Dissemination and Cochrane Handbook for Systematic Reviews of Interventions and recorded using the Cochrane Risk of Bias Tool.

Methods of Data Synthesis

Details of results on clinical effectiveness and quality assessment for each included study are presented in structured tables and as a narrative summary. The possible effects of study quality on the clinical effectiveness data and review findings are discussed. The 16 randomised controlled trials (RCTs) identified evaluated 14 different pair-wise comparisons. Therefore, there were insufficient data for most comparisons to carry out a standard pair-wise meta-analysis. However, the Technology Assessment Group (TAG) determined that the data identified were sufficiently homogenous to investigate comparative effectiveness of interventions via a network meta-analysis (NMA). The methods used for the NMA followed the guidance described in the NICE Decisions Support Unit's (DSU's) Technical Support Documents (TSDs) for Evidence Synthesis. In essence, an NMA assumes that each trial included in the network could have potentially included all treatments of interest but that some of these treatments are missing completely at random (MCAR). To illustrate this further, in a simple indirect comparison of three treatments A, B and C, the trials of A versus B and of B versus C are assumed to have been potentially trials of A versus B versus C but where one arm from each trial is MCAR. In this example, an estimate of the relative treatment effect of A versus C can be inferred using treatment B as a common comparator.

The TAG conducted an NMA for each network using a Bayesian Markov Chain Monte Carlo (MCMC) simulation in WinBUGS. The following were implemented for each analysis:

- Uniform priors (also called "flat" priors) were used.
- All outcomes were considered independent. For example, while overall survival (OS) and progression-free survival (PFS) might be correlated in advanced ovarian cancer, the degree of correlation is unlikely to be derived from summary trial estimates provided in published papers. As such, in the absence of individual patient data (IPD), the TAG took the pragmatic approach of assuming all efficacy and safety outcomes were independent.
- Results for all efficacy outcomes analysed were based on 50,000 iterations after a "burn in" of 30,000 iterations. For safety outcomes all analyses had a "burn in" of 30,000 iterations, with results based on 100,000 iterations.
- Summary effect estimates for OS and PFS were hazard ratios (HRs), while overall response rate (ORR) and all safety outcomes used odds ratios (ORs) as summary effect estimates.
- As a result of disparity in HRs reported in the identified trials, in terms of unadjusted HRs versus adjusted HRs, together with variation in adjustment factors, for consistency the TAG used only unadjusted HRs in the NMA.
- Any results taken forward into the economic model used the posterior sampling to retain the correlation between parameter estimates caused by their joint estimation from a single dataset.

However, the ability of the TAG to conduct NMAs was limited by the low number of trials identified (typically only one trial per treatment comparison).

See Section 4.1.5 of the Assessment Report for constraints imposed by the limited number of available trials. See Section 4 of the Assessment Report for additional information on clinical evidence analysis.

Cost-effectiveness

Independent Economic Assessment

As no single published study, or manufacturer's submission, simultaneously compared the cost-effectiveness of treatments relevant to the scope of this multiple technology appraisal (MTA), the TAG carried out an independent assessment and developed a *de novo* economic analysis.

Model Structure

The model structure employed by the TAG, to facilitate a comparison of the cost-effectiveness of the interventions and comparators outlined for this MTA, is derived from the cohort model developed in TA91 (see Figure 25 of the Assessment Report).

The TAG elected to use a cohort model approach rather than individual patient modelling. This approach was considered to be the most appropriate because, with the exception of platinum-free interval (PFI), there is limited evidence of the effect of individual patient characteristics/history on disease course. Furthermore, data were not available at a sufficiently disaggregated level in order to model at the individual level.

To capture the full costs and benefits associated with therapies for recurrent ovarian cancer, a lifetime time horizon was considered to be appropriate. In the base case analysis this is set as 15 years, because at this time point, over 99.9% of patients within the model have died. Furthermore, as per the NICE reference case, costs and benefits are discounted at a rate of 3.5% per annum, and an NHS and Personal Social Services (PSS) perspective was considered. The time horizon and discount rates used have been varied in sensitivity analysis.

See section 5 of the Assessment Report for additional information on cost-effectiveness analysis.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Care Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE Web site. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who Is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS

and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

Summary of Appraisal Committee's Key Conclusions

Availability and Nature of Evidence

The company for trabectedin submitted cost-effectiveness evidence as part of its submission.

The assessment group developed a de novo model.

Uncertainties Around and Plausibility of Assumptions and Inputs in the Economic Model

There was uncertainty around estimates generated by the assessment group's network meta-analyses that were incorporated into the model. The committee noted that no evidence was available for gemcitabine plus carboplatin, topotecan, and trabectedin plus pegylated liposomal doxorubicin hydrochloride (PLDH) for treating second and subsequent recurrences of ovarian cancer in women with platinum-sensitive disease. The recommendations are therefore limited to a first recurrence of ovarian cancer and do not stop clinicians and patients from considering these treatments for second or subsequent recurrences of platinum-sensitive ovarian cancer.

Incorporation of Health-related Quality-of-Life Benefits and Utility Values. Have Any Potential Significant and Substantial Health-related Benefits Been Identified That Were Not Included in the Economic Model, and How Have They Been Considered?

The committee did not draw any specific conclusions about the health-related quality-of-life benefits and utility values.

Are There Specific Groups of People for Whom the Technology Is Particularly Cost Effective?

None was identified.

What Are the Key Drivers of Cost-effectiveness?

The incremental cost-effectiveness ratio (ICER) estimates were most sensitive to the relative effect of treatment on overall survival.

Most Likely Cost-effectiveness Estimate (Given as an ICER)

For women with platinum-sensitive recurrent ovarian cancer, the committee agreed that:

- The ICER for paclitaxel plus PLDH compared with platinum alone was approximately £24,400 per quality-adjusted life year (QALY) gained.
- PLDH plus platinum was dominated by paclitaxel plus platinum in the fully incremental analysis but the committee accepted that the ICER for PLDH plus platinum compared with platinum alone was approximately £30,200 per QALY gained and it could also be considered cost effective.
- For women who cannot have platinum treatment, the ICER for PLDH monotherapy compared with paclitaxel monotherapy was approximately £23,700 per QALY gained.
- Gemcitabine plus carboplatin was extendedly dominated and excluded from the fully incremental analysis. The committee agreed that the ICER for gemcitabine plus carboplatin compared with platinum alone was £114,000 per QALY gained.
- The ICER for trabectedin plus PLDH compared with PLDH alone, as estimated by the assessment group and incorporating the updated patient access scheme, was above £70,000 per QALY gained.
- Topotecan was dominated and excluded from the fully incremental analysis.

For women with platinum-resistant or refractory ovarian cancer, the committee agreed that:

- The ICER for topotecan compared with PLDH was approximately £450,000 per QALY gained.
- Paclitaxel was dominated by PLDH, but the committee noted that the costs and QALYs associated with paclitaxel are similar to those of

PLDH and concluded that both could be considered cost effective.
- The additional analyses produced by the assessment group after appeal showing the impact of varying the drug cost for paclitaxel and PLDH did not change its conclusion that the costs and QALYs associated with paclitaxel and PLDH were similar.

How Has the New Cost-effectiveness Evidence That Has Emerged Since the Original Appraisals (Technology Appraisal 91 [TA91] and TA222) Influenced the Current (Preliminary) Recommendations?

For women with platinum-refractory or platinum-resistant disease, or who are allergic to platinum-based compounds, for whom PLDH and single-agent paclitaxel are considered inappropriate, topotecan is now not considered to be a cost-effective use of National Health Service (NHS) resources.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

Consultee organisations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination (FAD).

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

The Appraisal Committee considered clinical and cost-effectiveness evidence submitted by the manufacturers and a review of this submission by the Assessment Group. The main clinical effectiveness evidence came from randomised controlled trials. For cost-effectiveness, the Appraisal Committee considered economic models submitted by one of the manufacturers and by the Assessment Group.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate use of paclitaxel and pegylated liposomal doxorubicin hydrochloride (PLDH) in women with recurrent ovarian cancer to increase response to treatment, survival, and quality of life

Potential Harms

The summaries of product characteristics list the following as the most common adverse reactions associated with:

- Paclitaxel: infection, myelosuppression, neutropenia, anaemia, thrombocytopenia, leukopenia, bleeding, mild hypersensitivity reactions, neurotoxicity, hypotension, diarrhoea, vomiting, nausea, mucositis, alopecia, arthralgia and myalgia
- Pegylated liposomal doxorubicin hydrochloride (PLDH): anorexia, nausea, stomatitis, vomiting, palmar–plantar erythrodysesthesia, alopecia,

rash, asthenia, fatigue and mucositis

Qualifying Statements

Qualifying Statements

- The recommendations in this guidance represent the view of the National Institute for Health and Care Excellence (NICE) and was arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance are at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.
- Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the National Health Service (NHS) Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Implementation of the Guideline

Description of Implementation Strategy

- Section 7(6) of the National Institute for Health and Care Excellence (NICE) (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires clinical commissioning groups, National Health Services (NHS) England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.
- The Welsh Assembly Minister for Health and Social Services has issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 3 months of the guidance being published.
- When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraph above. This means that, if a patient has recurrent ovarian cancer and the doctor responsible for their care thinks that paclitaxel or pegylated liposomal doxorubicin hydrochloride (PLDH) is the right treatment, they should be available for use, in line with NICE's recommendations.

Implementation Tools

Foreign Language Translations

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Topotecan, pegylated liposomal doxorubicin hydrochloride, paclitaxel, trabectedin and gemcitabine for treating recurrent ovarian cancer. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Apr 27. 61 p. (Technology appraisal guidance; no. 389).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2016 Apr 27

Guideline Developer(s)

National Institute for Health and Care Excellence (NICE) - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Care Excellence (NICE)

Guideline Committee

Appraisal Committee

Composition of Group That Authored the Guideline

Committee Members: Dr Jane Adam (*Chair*), Consultant Radiologist, Department of Diagnostic Radiology, St George's Hospital, London; Professor Iain Squire (*Vice-Chair*), Consultant Physician, University Hospitals of Leicester; Dr Graham Ash, Consultant in General Adult Psychiatry, Lancashire Care NHS Foundation Trust; Dr Jeremy Braybrooke, Consultant Medical Oncologist, University Hospitals Bristol NHS Foundation Trust; Dr Gerardine Bryant, GP, Swadlincote, Derbyshire; Professor Aileen Clarke, Professor of Public Health and Health Services Research, University of Warwick; Dr Justin Daniels, Consultant Paediatrician, North Middlesex University Hospital; Dr Andrew England, Senior Lecturer, Directorate of Radiography, University of Salford; Dr Rachel Hobson, Formulary Pharmacist, NHS Wiltshire CCG; Dr Mohit Misra, GP, Queen Elizabeth Hospital, London; Ms Sarah Parry, Clinical Nurse Specialist - Paediatric Pain Management, Bristol Royal Hospital for Children; Ms Pamela Rees, Lay member; Dr Paul Robinson, Medical Director, Merck Sharp & Dohme; Ms Ellen Rule, Director of

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Financial Disclosures/Conflicts of Interest

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: National Institute for Health and Clinical Excellence (NICE). Paclitaxel, pegylated liposomal doxorubicin hydrochloride and topotecan for second-line or subsequent treatment of advanced ovarian cancer. London (UK): National Institute for Health and Clinical Excellence (NICE); 2005 May. 46 p. (Technology appraisal; no. 91).

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available for download in ePub and eBook formats from the NICE Web site .

Availability of Companion Documents

The following are available:

- Edwards SJ, Barton S, Thurgar E, Trevor N. Topotecan, pegylated liposomal doxorubicin hydrochloride, paclitaxel, trabectedin and gemcitabine for the treatment of recurrent ovarian cancer: a multiple technology appraisal. London (UK): BMJ-TAG; 2013. 574 p. Available from the National Institute for Health and Care Excellence (NICE) Web site .
- Topotecan, pegylated liposomal doxorubicin hydrochloride, paclitaxel, trabectedin and gemcitabine for treating recurrent ovarian cancer. Resource impact report. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Apr. 3 p. (Technology appraisal guidance; no. 389). Available from the NICE Web site .

Patient Resources

The following is available:

- Topotecan, pegylated liposomal doxorubicin hydrochloride, paclitaxel, trabectedin and gemcitabine for treating recurrent ovarian cancer. Information for the public. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Apr. 3 p. (Technology appraisal guidance; no. 389). Available in English and Welsh from the National Institute for Health and Care Excellence (NICE) Web site . Also available for download in ePub and eBook formats from the NICE Web site .

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